EXHIBIT 1

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patients."
Do you see that?
A. Yes.
Q. Calling this a clinical entity means it exists, correct?
A. I think I've agreed that there is this existence of an association in a small number of cases. You keep asking me to equate that with cause, and you can't do that.
MR. SLATER: Move to strike from "you" forward.
Q. This section states in part after what I just read, "Patients' symptoms were severe, usual, and unexplained after extensive evaluation. In such circumstances, it is important to consider medication side effect in the differential diagnosis regardless of how distant time of initiation of medication to the onset of symptoms and how removed the constellation of symptoms may be from the primary pathway being targeted."
Do you agree with that statement?
A. As a generalization, sure.
Q. "Other medications such as

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fenfluramine, phentermine, and bisphosphonates have been found to have serious side effects months to years after starting therapy and affecting organs distant from the site of target." And then it talks about a New England Journal of Medicine publication on that issue, correct?
A. Correct.
Q. And then at the bottom of that paragraph it says, "OAE, like the above historical examples, highlights the importance of considering medication side effects in patients with unusual symptoms and unrevealing diagnostic evaluations."
Do you see where I just read?
A. Yes.
Q. Do you agree with that statement?
A. Yeah, and I think they're specifically saying this is unlike those, because those are historical examples with fact, and here they're talking about these case reports. That citation --
Q. Doctor, it says "OAE, like the above historical examples, highlights the importance."

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They're analogizing it based on the fact that you have this delay between using the medication and the onset of symptoms. That's what they're talking about there, isn't that true?
A. They're saying that delays happen, and that you should consider medication side effects.
Q. The fact that with olmesartan, the patient's symptoms will have an onset of variable time periods after initiation of the drug therapy, that is not a reason to reject the condition of olmesartan enteropathy, correct?
A. Correct.
Q. Look at Page 6 of 8, the left-hand column, about halfway down the second full paragraph, it says, "Although the risk of developing OAE in the setting of celiac disease is not known, patients thought to have underlying celiac disease can be affected by OAE."
Do you see what I just read?
A. Yes.
Q. Do you agree that that's -- that it's a correct statement?

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A. I think it's a speculation. There's no citation of data supporting that, there's no data supporting that that I'm aware of in the literature. This is a speculation in a discussion where you're allowed to make speculations.
Q. A patient could have celiac disease, underlying celiac disease, and develop olmesartan enteropathy, as a matter of physiology in medicine that could happen, correct?
MR. PARKER: Objection.
A. Are you trying to ask if olmesartan can prevent celiac disease from happening? I doubt it.
BY MR. SLATER:
Q. I wasn't asking that at all.
A. Can you rephrase your question?
Q. A patient could have underlying celiac disease and then could go onto olmesartan and could end up with symptoms of olmesartan enteropathy, there's no reason why they couldn't have underlying celiac disease and have olmesartan enteropathy? The two could occur,

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correct?
A. I think if you read this article, they'll tell you that if a patient has celiac disease, they don't have olmesartan-associated enteropathy, that that's a diagnosis that you need to exclude. So no, that's not -- there's no data for that.
Q. A patient with underlying celiac disease can, as they state here, be affected by olmesartan-associated enteropathy? That physiologically could occur, correct?
MR. PARKER: Objection.
A. Theoretically.
BY MR. SLATER:
Q. That's what they state, right?
A. They're saying it's theoretical. The first half of that sentence says, "The risk of developing OAE in the setting of celiac disease is not known," meaning we don't know if there's any risk whatsoever.
Q. Do you have an opinion one way or another on that question?
THE VIDEOGRAPHER: We're having a tough time understanding you, sir.

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Q. Do you have an opinion on that question one way or the other to a reasonable degree of medical certainty?
A. My opinion is that there's not sufficient data to make any judgment.
Q. Not enough data to answer that question yet?
A. Right.
Q. Look at Page 7 of 8, please. Five lines down it says, "It would seem reasonable to hold olmesartan much earlier in the natural history of the illness rather than assuming other diagnosis first in order to limit worsened symptoms leading to nutritional deficiencies and requiring a greater level of care and more extensive diagnostic evaluations."
Do you agree that's a reasonable clinical recommendation?
A. I'm just trying to find where you're reading.
MR. PARKER: I think it's over here under "Conclusions."
A. Okay. Hold on.
(Witness reviewing document.)

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A. Sure. If your patient is going to get better if you remove olmesartan, which happens in these really rare cases, there's that association, changing to a different antihypertensive is pretty simple. So I would do that, it's free. It doesn't harm the patient. It may help the patient. The rest of the workup for celiac disease takes time. Why wouldn't you do that?
BY MR. SLATER:
Q. Okay. We can put that article aside. Just looking in the grab bag to see what's next, Doctor.
A. Okay.
Q. Why don't we talk about the Marietta immunopathogenesis article.
A. Okay.
Q. We probably have to get to that at some point. You're familiar with this study?
A. Yes.
MR. SLATER: Let me just see if I have it in my pile here to mark as an exhibit. It's document 9, Peter.

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(Whereupon, Turner Exhibit Number 14, Marietta, et al article titled Immunopathogenesis of olmesartan-associated enteropathy, was marked for identification.)
MR. SLATER: Let's just mark document 5 as Exhibit 15.
(Whereupon, Turner Exhibit Number 15, Rubio-Tapia, et al article titled Severe Spruelike Enteropathy Associated With Olmesartan, was marked for identification.)
BY MR. SLATER:
Q. Doctor, just for the record, we've talked about the Rubio-Tapia 2012 article several times. I've marked it as Exhibit 15. I just want to confirm for the record, is that the article we've been discussing when we've talked about that?
A. If we talked about the 2012 Rubio-Tapia article, that's the one we were discussing.
Q. Okay.
A. I think we discussed an article by

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Rubio-Tapia.
Q. Well, we've talked about that throughout the deposition. This is your understanding that this is the article, Severe Spruelike Enteropathy Associated With Olmesartan, we've discussed that during the deposition, correct?
A. We've discussed this, but we've also discussed other articles published in the Mayo Clinic Proceedings, other articles published in 2012, and other articles by Rubio-Tapia. This is the only article that meets all three of those criteria.
Q. Okay. Now, let's go to Exhibit 14. You're familiar with this article and this study, correct?
A. Yes.
Q. Okay. Now, let's look at the beginning of the article where it says "Background." It says, "Olmesartan-associated enteropathy is characterized by diarrhea, nausea, vomiting, abdominal pain, weight loss and severe sprue-like enteropathy, all of which are resolved after discontinuation of olmesartan

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medoxomil."
Do you see where I just read?
A. Yes.
Q. You would agree with me that where all of those symptoms are resolved after the drug is discontinued, that fits the diagnostic criteria for this condition, correct?
A. That fits what people generally are referring to as olmesartan-associated enteropathy.
Q. Let's look, if we could, at Page 4 of this article.
Give me one second. Bear with me for a second, I just want to find the spot.
All right. Actually go to Page 11, I'm sorry. At the very top of Page 11, the left-hand column, it says, "In summary, a small number of patients will develop enteropathy in response to olmesartan medoxomil; this enteropathy is not gluten dependent, and both the stomach and colon of many OAE patients are also affected in addition to the small intestine."
Do you see that?

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A. I do.
Q. So in his statement, the authors, including Dr. Murray, are calling the entity OAE and stating that the patients who have this condition will develop the enteropathy in response to using the medication, correct?
A. I think that's what they're writing. I think it's a reach.
MR. SLATER: Move to strike "I think it's a reach."
Q. One question on this article. One part of what they did was they used Caco-2 cells to try to study this condition. That's part of what they did in this experiment, correct?
A. Correct.
Q. Caco-2 cells are used to study small intestine pathology, histopathology, that is something that is done, correct?
A. I don't know anybody using them to study histopathology. But mechanisms of disease, sure.
Q. Let me restate the question. That one I'll give you was a bad question. I'll buy you a beer for that one. And Bruce, too, because he

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needs one.
MR. PARKER: I sure do.
A. The videographer would like one, too.
BY MR. SLATER:
Q. What, sir?
A. The videographer.
Q. If you tell me a liquor store, I'll call it in with my credit card.
A. It's too bad you didn't bother flying in, there's a great brewery just down the street.
MR. PARKER: All right, guys. Let's go.
BY MR. SLATER:
Q. I know the brewery. I know right where you are.
Okay. Let me do it this way so we can make sure the phrasing is to your liking.
Caco-2 cells were used in the study, correct?
A. Correct.
Q. They were used to study a small intestine condition, correct?
A. Yes.

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Q. That is something that is accepted to be done in the scientific community, correct?
A. Correct.
Q. If somebody were to criticize the use of Caco-2 cells here and say why would you use colonic cancer cells in a small intestine study, that would not be a reason to reject the findings, correct?
A. When properly done, and that's a huge caveat, but when properly done, Caco-2 cells differentiate much more like small intestines, so it would not be an adequate criticism. But that assumes that you're using your Cacos in a good condition.
Q. In the study, the investigators are studying or trying to determine the microscopic mechanisms for this condition that they're studying, correct?
A. I would object to the term microscopic. Maybe they're trying to determine molecular mechanisms.
Q. Let me rephrase the question.
In this study, the investigators are studying the molecular mechanism for this entity

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that they're studying, correct?
A. Correct.
Q. And ultimately, what is your understanding of what their conclusion was?
A. It's a crazy conclusion. This is just a terrible study.
MR. SLATER: Move to strike. Doctor, move to strike.
Q. So let's just answer my question, and then you can call Dr. Murray your buddy and tell him it's a crazy study and it's a piece of garbage, I assume you're going to do that after we get done here, but let's just stick with my question.
A. I don't usually try to create arguments with people. I think if Joe and I were talking and I told him it was a crappy study and why, he'd agree with me. I'm trying to find where they say, but they essentially conclude that IL-15 --
Q. Let me stop there.
MR. PARKER: Whoa, whoa, whoa.
MR. SLATER: I move to strike all the colloquy. I just want to get a clean answer.

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MR. PARKER: No, no, Adam, you've told me repeatedly I cannot interrupt your experts in the middle of an answer. So let the witness finish his answer, then you can follow up with another question.
A. I think what they've essentially shown is that there's some increased fluorescence with their anti-L-15 antibody, and some ill-defined changes of ZO-1 that they're somehow attributing as having something to do with olmesartan and enteropathy.
Q. Did the study show increased levels of IL-15 based on exposure to olmesartan?
A. No.
Q. Did the investigators running the study think that they saw increased levels of IL-15?
A. It looks like they might have, shockingly enough.
MR. SLATER: Move to strike "shockingly enough."
Q. In order to have a biologically plausible mechanism, one does not need to establish the mechanism on the molecular level

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for this or any other condition, correct?
A. Correct.
Q. As you understand it, what is the understanding among those who believe this entity exists as to what the biologically plausible mechanism is?
A. There really isn't one. They've drawn analogy to celiac disease wherever possible, and have done immunostains that are sort of self-evident from the traditionally hemotoxin and eosin morphology, but they really don't have a plausible biological explanation.
Q. Have you seen statements in the medical literature that indicate that the olmesartan initiates an immune-mediated response that causes cellular changes that leads to inflammation and villous atrophy, and then the symptoms that are seen with this condition?
A. That's one of the things that's been thrown around, yes.
Q. If accurate, that would be a -- if accurate -- let me rephrase it.
If that is accurate, that would be a plausible biological mechanism, correct?

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A. Sure. If that happened, it would be a plausible biological mechanism, absolutely.
Q. Do you know whether or not anybody at Daiichi proposed doing a similar study to what they saw here with Caco-2 cells, or any other type of study whatsoever, to try to replicate or disprove this study?
A. I think if they proposed that, it would be foolish, and a study like this one would never be worth doing. I don't know what -- I can't tell you what Daiichi did. I'm not involved with Daiichi.
Q. What study would you propose to do to prove or disprove what the molecular mechanism is? If you wanted to prove that, how would you do that study?
MR. PARKER: Objection.
A. I think that's a hard study to do. I think this is definitely the wrong way. If you do this study, you are at face value assuming that Caco-2 cells should respond in the same way as these rare patients.
So let's start with the assumption that rare patients do have something that's

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induced by olmesartan that is enteropathy. I don't agree that that's been proven, but let's start with that assumption. You're going to assume that this generic epithelial cell that presumably represents the 99.99 percent of patients who don't have any problems with olmesartan is the appropriate model, and then you by your own self just said it triggers immune-mediated responses. Where are the immune cells? There aren't any.
If we want to then get into the data points they have here, this is technically -- I mean if an undergraduate in my lab showed me this, I would tell them what they did wrong and tell them to go try it again. This is just abhorrent technique throughout this study in the Caco-2 parts. And I would tell Joe that to his face.
Q. If you wanted to try to prove or disprove whether olmesartan medoxomil causes sprue-like enteropathy, what would you do to structure a study?
A. All right. If you want to test parts of that hypothesis, okay, let's start there,

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let's say you believe that this Caco nonsense is true -- is he listening or is he doing something else?
MR. PARKER: Go ahead, go ahead.
A. So let's say you think this is right, the appropriate thing to do would be to get biopsies from people who suffered from, quote, olmesartan-associated enteropathy, and controls. You can grow intestinal epithelial cells from those patients, and now do that assay and ask if there's a selective effect of olmesartan on the people who got sick that you're attributing to olmesartan versus the people who seem to benefit from olmesartan and have no disease. That would be a place to start if you wanted to look at direct epithelial injury, or, you know, or activation of IL-15 production, or anything like that.
BY MR. SLATER:
Q. Do you agree, disagree, or not have an opinion yet based on the state of science that olmesartan medoxomil when exposed to the small intestine causes in some patients villous atrophy?

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A. I don't think there's sufficient evidence to conclude that it causes.
Q. Is it still an open question?
A. I think it's an open question. It's very hard to prove a negative.
Q. The prevailing understanding in the medical literature is that yes, in some patients the exposure of olmesartan medoxomil leads to villous atrophy in some patients, correct?
MR. PARKER: Objection. Asked and answered.
A. I think the prevailing opinion is that when you're treating patients, if you think this is a possibility, remove olmesartan, if they do better, call it a win. I don't think that's the same as concluding causation in a rigorous manner.
BY MR. SLATER:
Q. What I'm asking you is this. Those scientists and physicians who have been involved in actually treating patients with this condition and studying the condition, there is a consensus among them that in some patients olmesartan medoxomil leads to villous atrophy in

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some patients, correct?
MR. PARKER: Objection.
A. They've described this association and described in individual cases improvement upon withdrawal of olmesartan.
MR. SLATER: Why don't we take a break for a couple minutes.
MR. PARKER: Sure.
MR. SLATER: Let me organize some notes, some documents.
I need to know how much time I'm at, too, after we go off the video.
THE VIDEOGRAPHER: Sure. Going off the record. The time is 2:43.
(Whereupon, a recess was taken.)
THE VIDEOGRAPHER: Back on the record. The time is 2:58.
MR. SLATER: You have to give me a second. I actually wasn't ready to start.
THE VIDEOGRAPHER: I'm sorry. I'll just go off the record. Going off the record. The time is 2:59.
(Pause.)
THE VIDEOGRAPHER: Back on the record.

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The time is 2:59.
MR. SLATER: Let's pull out document 4, Peter, please.
(Whereupon, Turner Exhibit Number 16, Choi and McKenna article titled Olmesartan-Associated Enteropathy. A Review of Clinical and Histologic Findings, was marked for identification.)
BY MR. SLATER:
Q. Okay. Doctor, this is one of the articles I believe you listed on your reliance list, correct?
A. Yes.
Q. Exhibit 16?
A. Yes.
Q. It's titled "Olmesartan-Associated Enteropathy. A Review of Clinical and Histologic Findings," correct?
A. Correct.
Q. And it looks like it was published in the Archives of Pathologic, or Pathology Laboratory Medicine, right?
A. Right.

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Q. Is that a journal that you're familiar with?
A. Yes.
Q. Is it a respected journal?
A. It's pretty low end.
Q. Have you ever published an article in it?
A. I don't think so.
Q. Did you ever try and they wouldn't take it because it was too high level?
A. No. I don't think they'd do that.
Q. They don't turn down articles for being too good?
A. I'm sure they do reject some articles.
Q. Okay. Let's look at this article. And starting with the second paragraph, it's giving a bit of an overview, and the last sentence of the second paragraph says, "There are approximately 100 cases currently reported in the English-language literature that support olmesartan-associated enteropathy as a distinct clinical entity."
Do you see where I just read?
A. Yes.

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Q. As that entity is described in the literature, would you agree that it is considered to be a distinct clinical entity?
A. I think they've said it really well here. They say that support that conclusion, and I think that's exactly right.
Q. Before we get into the meat of the article, let's go to the conclusion. It says, "Olmesartan-associated enteropathy is a rare cause of severe enteropathy that should be considered in the differential diagnosis of patients with unexplained chronic diarrhea who are taking olmesartan-containing medications."
Do you see what I just read?
A. Yes.
Q. So these authors conclude that olmesartan causes this condition, this enteropathy, correct?
A. I think that's a poorly phrased sentence. They don't cite anything to document that, they don't present any original data here, so it's a little hard to come -- how they come with that conclusion, but it is what they say.
MR. SLATER: Move to strike.

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Q. Is that what they say?
A. That's what their words say.
Q. Let's go back to the beginning of the article. Actually, let's go to the second page, Page 1243. There's discussion on Page 1243, there's a heading that says "Microscopic Findings."
Do you see that?
A. Yes, I do.
Q. And they talk in the last paragraph of that section about Lagana, et al, which is one of the articles you reviewed, which is reference 221, correct?
A. Yes.
Q. It says in part, this is towards -- just past the halfway point of that paragraph, "No single histopathologic finding was statistically more frequent in patients taking olmesartan compared with age and sex-matched controls. The authors, however, noted a trend toward significance in the finding of at least one sprue-like microscopic feature in the patients taking olmesartan but not in those taking other ARBs, and they raised the

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possibility that there may be a spectrum of changes with olmesartan use."
Do you see what I just read?
A. Yes.
Q. That's another summary of some of the findings that were documented in that article, right?
A. Well, that's almost a verbatim quote of the descriptions that were given in that article, yes.
Q. This article then says, "This study, however, was limited by small sample size and lack of follow-up information regarding patient outcomes."
Would you agree with that statement?
A. I would agree that that's just the beginning of the limitations of that study, but yes, I would agree.
Q. Now go to the "Comment" section. It says, "Establishing a causal relationship in drug-induced enteropathy is difficult. Although deliberate rechallenge with olmesartan to prove causality following withdrawal and symptomatic improvement is not usually attempted given the

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severity of symptoms, symptomatic recurrence following reintroduction of olmesartan has been documented," and then they cite the Gallivan and Brown article that we went through earlier today, or the letter, correct?
A. Correct.
Q. They next cite to the DeGaetani article, which is from the Columbia group in the celiac center, correct?
A. Correct.
Q. Those doctors are specialists in the treatment of celiac, correct?
A. Correct.
Q. And the celiac center at Columbia is a nationally recognized and highly respected center, correct?
A. I'd say Dr. Green is and, therefore, the center is.
Q. Do you know the other doctors?
A. I know some of them, but I think if Dr. Green left it would lose most of its stature pretty quickly.
Q. Do you know Dr. Green?
A. I know Dr. Green.

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Q. Do you know that he's published articles that actually state that olmesartan causes sprue-like enteropathy?
A. Yes, I do.
Q. He's considered to be a leading authority on the subject, correct?
A. He is an absolute authority on clinical management of patients with celiac disease, and I would attest to that any day.
Q. Let me ask you a question. When you were asked to be an expert in this case, did you consider saying, you know, I haven't done any work related to olmesartan at all in my career, maybe you should find somebody who actually has some experience with this. Did you say that to anybody?
A. No.
Q. The DeGaetani article is cited in this Comment section. You're familiar with that study, correct?
A. Yes, I am.
Q. And that had to do with patients who had been -- essentially they couldn't really diagnose them with a specific condition, they

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didn't -- they weren't having any sort of improvement off a gluten-free diet, and then when the subject of this olmesartan-associated enteropathy came out and they went and contacted them, a whole host of these patients got better when they went off olmesartan. That's essentially what happened, right?

MR. PARKER: Objection.

A. Well, they were also on immunosuppressants.

BY MR. SLATER:

Q. Well, they were on immunosuppressants, but they continued to have symptoms when they were on immunosuppression, correct?

MR. PARKER: Objection.

A. So it says 80 percent received immunosuppressive agents, and 86 percent of those showed symptoms --

MR. PARKER: Slow down.

A. I'm sorry. I'm very sorry. I'm most of the way down the left column on Page 650, actually why don't I start a little higher, just -- well, it doesn't matter. Let's start about three-quarters of the way down, the last

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word in the line says 80 -- it says, "80 percent received immunosuppressive agents, and 86 percent of these showed symptomatic improvement in follow-up data."

Q. Do you see the center column of the DeGaetani article where at the bottom it says, "We identified 16 patients taking olmesartan, of whom 68 percent had increased epithelial collagen in addition to villous atrophy. Upon discontinuation of this medication, all 15 patients on whom we had follow-up data improved symptomatically, no longer requiring immunosuppressive therapy if they had previously been on it, and some have resumed a gluten-containing diet with no recurrence of symptoms."

Do you see that?

A. Yes, I do.

Q. So they got better off the olmesartan even when the immunosuppressive therapy had been stopped, and in some cases even when they resumed gluten. That's a strong argument that at least some of them had this sprue-like enteropathy due to the olmesartan, correct?

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MR. PARKER: Objection.

A. It implies that there's a lot going on. It also implies that the cases identified here are very different from the cases identified in the 2012 Rubio-Tapia article that we were talking about. Those patients all failed immunosuppressants. These patients responded to immunosuppressants. So Murray wouldn't have included these patients in his group. So suddenly we're expanding what we're going to expand what we're going to call olmesartan-associated enteropathy, and it becomes really fuzzy. It looks like this went on over a period of time.

BY MR. SLATER:

Q. Let's put aside the label for a second. For at least some of these patients, would you agree that their gastrointestinal illness as defined in this article was caused by olmesartan?

A. No.

Q. Not one of them?

A. I don't think there's any evidence that olmesartan caused it.

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Q. Do you have an opinion of what was causing their gastrointestinal illness if it was not olmesartan?

A. I don't. It could certainly be idiopathic.

Q. Let's talk about the Rubio-Tapia patients, the 22 patients. Would you agree with me that at least some of them, putting aside the label, suffered from severe diarrhea, weight loss, and had villous atrophy as a result of using olmesartan?

A. Again, I think you're trying to associate recovery and withdrawal of olmesartan with cause, and I don't think there's data to support that mechanism, or that concept.

MR. SLATER: Move to strike.

Q. With regard to the Rubio-Tapia patients, the 22 patients, would you agree that at least for some of those patients their clinical symptoms of severe diarrhea, weight loss, and villous atrophy was caused by olmesartan?

MR. PARKER: Objection.

A. No.

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BY MR. SLATER:
Q. What was causing their severe diarrhea, their weight loss, and their villous atrophy if it wasn't the olmesartan? Do you have an opinion?
A. I don't know.
Q. If in the Rubio-Tapia study they had deliberately rechallenged those patients in a controlled environment, and they had a resumption of their symptoms and resolution, for those patients would you say, yes, that patient, their syndrome was caused by the olmesartan?
A. Are we agreeing that it would be randomized, a controlled trial?
Q. I'm talking about the 22 patients.
A. Right.
Q. If they rechallenge those 22 patients who had gotten better, if they then got sick again when they were rechallenged with olmesartan, would you say for those patients, okay, look, they got better after they went off it, now they got sick again when they went back on it, I will agree for those patients the illness was caused by olmesartan?

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A. And you're talking about this exact description of what's available here?
Q. The Rubio-Tapia article.
A. No, I don't think that's sufficient evidence that olmesartan caused their enteropathy.
Q. So a dechallenge and a rechallenge in a patient, that's not enough -- along with the other information in that study, that would not be enough for you to say likely causation, do I understand you correctly?
A. You're using the terms dechallenge and rechallenge loosely, and I don't -- I think in that study particularly they went to lengths to say we don't think this proves it. So I can't think it proves it either.
Q. Isn't it important when you're publishing the first article identifying an entity, the first time it's ever been specifically identified in the literature, to be prudent and say, as they did, there's an association, we don't think it's a chance association, but we're going to need to study this more? Isn't that a conservative way to

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approach it?
A. I think it reflects on the quality of your data.
Q. The question is this. If they had deliberately rechallenged those 22 patients, and in those patients who had resolved their problems when they were off the drug, if their symptoms came back as described in the study, in the article, you don't think that's enough to say, okay, in those patients I can agree the olmesartan was causing this syndrome?
A. No.
Q. Fine.
Is the only rechallenge that you think is enough is a randomized controlled rechallenge?
A. Okay, so we have to specify. Are we talking about general causation, or are we talking about a specific patient?
Q. General causation.
A. I don't think anything in an individual patient can tell you about general causation in a population.
Q. Okay. In the specific patients, would

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that be enough to tell you causation in the specific patients?
A. If it was randomized controlled challenge/rechallenge, then I would say yes.
Q. Is there some peer-reviewed accepted scientific literature or standard that says the only rechallenge that can be relied on to establish causation is a randomized controlled rechallenge?
A. There is plenty of literature on placebo effect, and in general that sort of -- those sort of data are never considered good enough for causation. General case reports and things like this are considered the lowest level of evidence, and really need to be supported by epidemiologic studies, animal studies, mechanistic studies, anything to really give credence to it.
Q. Tell me about some examples of randomized studies that have been done to study rare adverse drug reactions.
A. I think that's where many of them are picked up, is in large randomized studies.
Q. Many rare -- rephrase.

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Many rare adverse drug effects are picked up in case reports, correct?
A. Initially.
Q. Okay. Did anybody actually commission a randomized controlled study to try to study sprue-like enteropathy?
A. With that express goal as the primary endpoint, no.
Q. Are you an epidemiologist?
A. No, I am not.
Q. Okay. Do you plan to provide epidemiologic opinions in this litigation?
A. No.
Q. Going back to Exhibit 16, the Choi/McKenna paper, turn, if you would, to Page 1245, the top left corner. It talks about the Greywoode study.
Do you see that?
A. Yes.
Q. If you go down to the last sentence of that paragraph, it says that that "study was limited, however, by the small number of patients taking olmesartan: 22 patients (1 percent) in the esophagogastroduodenoscopy group

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and 83 patients (0.7 percent) in the colonoscopy group."
Do you see that?
A. Yes.
Q. Do you have an understanding as to whether, due to the small number of patients, whether or not the study was powered sufficiently to actually pick up any difference in the two groups?
A. My expectation is it probably wasn't sufficiently powered. But, again, I'm not an epidemiologist, and am not the person to assess that mathematically.
Q. Based on that, would it be correct that you would not want to rely heavily on the findings one way or the other from that study due to the fact that it's likely not sufficiently powered to study this question?
MR. PARKER: Objection.
A. It's probably not, but it has more patients than the Lagana study we were talking about, and it has the same number of patients that were reported in the Rubio-Tapia 2012 paper. So while it's likely not sufficiently

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powered, and I wouldn't take it as evidence, strong evidence, either way, I think it again is -- if you're going to start putting things on either sides of a balance, as you've suggested and made the analogy, this goes on the side that says there's no association.
BY MR. SLATER:
Q. If you were only going to put into the balance studies that were sufficiently powered to give information, you wouldn't put this into the balance, correct?
A. I think if you're going to do that, I would consult an epidemiologist. But I would probably not include any of the studies, with the exception of Basson, Padwal, and ROADMAP.
Q. Well, we just went through ROADMAP. If ROADMAP is not sufficiently powered, you wouldn't consider that from an epidemiologic -- rephrase.
We talked about ROADMAP. If that's not sufficiently powered, you wouldn't include that either?
A. Isn't that what I -- that's what I just said. I just said I would exclude.

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Q. I thought you said you would include.
A. No, I said I would exclude pretty much everything we've talked about, if we're talking about sufficient statistical power, and I would consult an epidemiologist about those three studies that I mentioned, because I'm not in a position to analyze the math and see -- ad be able to state definitively were they sufficiently powered. But what I would conclude is that pretty much everything else that we've talked about is case reports, and is not sufficiently powered.
You asked me earlier if the case reports all go on the side of olmesartan does cause enteropathy, and I said yes. But if we're going to use that low bar of how we pile things up, then the Greywoode study certainly must go on the other side. It's at least as good as the case reports.
Q. Do you have the Lagana study handy, the abdominal pain?
A. Yes.
MR. TURNER: I'm sorry. I missed that. What study?

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THE WITNESS: Lagana.
BY MR. SLATER:
Q. Do you have that handy?
A. I do.
Q. Let's look at Table 2. And Table 2, you have on the left side the olmesartan patients versus matched controls, and on the right side users of other ARBs and match controls, correct?
A. Correct.
Q. If you compare at the very bottom of the columns on the left for olmesartan, it said 10 out of 20 had one or more sprue-like features, and 4 out of 20 of the matched controls --
THE STENOGRAPHER: I'm sorry, I didn't hear that.
MR. SLATER: It's okay. I'll start over.
Q. If you look at the left-hand side of the table with the olmesartan users, at the bottom of the left column it says 10 out of 20 of the olmesartan users had one or more sprue-like features, and on the right-hand side

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it says of the matched controls 4 out of 20, and the p-value is .1. Correct?
A. Correct.
Q. And the authors just below that said that they demonstrated a trend towards sprue-like enteropathic changes in individuals taking olmesartan compared with controls. That's what they state, correct?
A. That's what they wrote.
Q. That's a correct statement as to the .1 p-value, that statistically -- and if you're not comfortable answering you can tell me, but statistically .1 would represent a trend but would not reach statistical significance, correct?
A. I don't think that's true.
Q. Now, let's look at this. The right-hand side, the other ARB analysis, comparing the other ARB users, 9 out of 20 had one or more sprue-like features, correct?
A. Yes.
Q. For the matched controls on that side of the ledger, 12 out of 20 had one or more sprue-like features, correct?

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A. Correct.
Q. And the p-value comparing the other ARB users to their matched controls is .34, correct?
A. Correct.
Q. That .34 number has nothing to do with the olmesartan users, it only is with -- relates to the other ARB users versus their matched controls, correct?
A. Correct.
Q. The trend that they referred to just below is a comparison of those taking olmesartan to their matched controls, and they based it on the .1 p-value. That's what that statement is based upon, correct?
A. Yes.
Q. Okay. Let's look at Basson. Do you have that handy? We are blowing through the literature here, Doctor. I'm going to tell you, you might owe me a beer.
A. Yes, I have it.
Q. Okay. What we should do is let's take Basson, and we're going to compare that a little bit at some point with Padwal. How does that

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sound for a plan?
A. Sounds good.
Q. Tell me when you're there.
MR. PARKER: I think we're all set.
BY MR. SLATER:
Q. Okay. The Basson study is a study of a French national health insurance claim database, correct?
A. Correct.
Q. I just want to start off looking at Table 2 in Basson. Do you see Table 2?
A. Yes. I'm sorry, I'm looking at Table 3. Yes.
Q. Table 2 is titled "Table 2: Risk Over Time Descriptive Data," correct?
A. Correct.
Q. And for the olmesartan users, the number of patient years is 860,894, right?
A. Right.
Q. And there were 48 events identified, right?
A. Right.
Q. And the events were defined as hospitalization for intestinal malabsorption and

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celiac disease. That's what they were looking for, right?
A. I think it was "or celiac disease," but yes. Is that right? Was it "or celiac disease"?
Q. Well, do you have an understanding of what they were looking at? I'm looking at the study, and on the next column, "Discussion," it talks about intestinal malabsorption and celiac disease, but if you think they were looking at something different, tell me.
A. No, I think those are the two things they looked at. I don't think they looked for patients that had both necessarily, they looked -- to be included in the study, a patient had to have one.
Q. We were talking past each other. The 48 events listed would be patients that were hospitalized either for intestinal malabsorption or celiac disease, correct?
A. Correct.
Q. Now, you can hold that page, or whatever you want. If we go to Padwal, can you go to where the number of patient years is set

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forth in Padwal? It's Table 2 again.
A. Yes.
Q. And for GI disease-related hospitalization, how many patient years was at issue there?
A. For the number -- for GI disease-related hospitalizations, it's 17,647.
Q. They found 498 events. But what were events defined as in Padwal?
A. Padwal had a much looser definition. Padwal was all gastrointestinal-related admissions, so that would include colon cancer, celiac disease, anything.
Q. Have you ever done the math to try to figure out, based upon Basson, how many of those events found in the Padwal study would -- if you have a proportionality, how many of those would actually be intestinal malabsorption or celiac disease? Have you ever tried to use the numbers, and compare them, and do that calculation?
A. I don't think you can. They don't have those data here.
Q. It's not something you've looked at,

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correct?
A. Again, I actually thought about those things when I looked at this paper, but I don't think there's sufficient data to do those calculations.
Q. Do you have an opinion as to whether or not the sample size in terms of patient years in Padwal was sufficient to identify events that would be attributable to olmesartan --
A. I do not.
Q. -- that would correlate to malabsorption or sprue-like enteropathy? Did you ever do that calculation or analysis?
A. No, I did not. There's fundamental differences in design here that even a non-epidemiologist can recognize.
As long as we're talking about Basson, we were discussing statistical significance, you might look at Table 3 and note that they reported a p-value of .09, which is less than .1, and they don't anywhere pretend that that has any significance or a trend.
Q. Look actually right next to Table 4 on Page 5 in the right-hand column. It says right

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next to it, "However, caution is needed to interpret these values as this study was not aimed to measure the incidence of olmesartan-associated enteropathy, but rather to estimate the strength of the association between olmesartan and severe forms of enteropathy and malabsorption. As a consequence, this study underestimates the true incidence and only provides the incidence of the most severe forms of olmesartan-associated enteropathy."
Do you see that?
A. I do.
Q. You have no reason to disagree with that, correct?
A. From my level of understanding, I would say that that's not entirely accurate. I would say that this study may underestimate, may overestimate, they don't have the data to say one way or another.
Q. You're not in a position to form an opinion on that, that's not your specialty, correct?
A. It's not my specialty.
Q. At the very bottom of Page 5 of

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Basson, they say, starting on the second to last line --
A. Wait, what --
Q. I'll start over.
On Page 5 of Basson, right below where I just read, the very bottom of the page, Page 5.
A. Yes.
Q. Second to last line, "Patients treated with olmesartan should be informed about the risk of this complication and should be advised to seek medical attention if they experience GI symptoms."
You don't disagree with that, right?
A. I don't disagree with that. I think that's a conservative approach.
Q. In performing your analysis, did you try to evaluate every rechallenge you could find in the peer-reviewed literature?
A. I did.
Q. That was discussed in the peer-reviewed literature?
A. Yes, I did.
Q. Is it your testimony that you didn't

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see any rechallenges discussed in the peer-reviewed literature that you were comfortable relying upon as valid evidence?
A. I don't think a single patient rechallenge could be taken as evidence of general causation first. In terms of specific causation, it could be if it were done in a controlled manner, but really there's, in these case reports, there's very little data provided. It just says things like then the patient started retaking it, or then we had them retake it. But it doesn't tell you what else is going on in the background, and so I don't think you can conclude that.
Move to strike?
MR. PARKER: Don't do his job for him.
BY MR. SLATER:
Q. Sure, move to strike. I don't want to disappoint you.
A. Sorry.
MR. PARKER: It's getting late. Let's just stay on track here.
BY MR. SLATER:
Q. Patients, case -- well, let me ask you

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this question.
There are a number of rechallenges documented in the peer-reviewed literature, correct?
A. Uncontrolled rechallenges, yes.
Q. They're not just one, there's a number?
A. Yes.
Q. Correct?
A. Yes.
Q. Taken together, you must agree that there is significance to the number of rechallenges documented, even if they're uncontrolled, there is some significance to that, and it must weigh in the analysis, correct?
A. You need to know what you're pulling from. If you're cherry-picking just the cases where rechallenge was positive, then you can't conclude that. If you tell me that that represents 10 percent of the rechallenges and 90 percent rechallenge didn't do anything, then you would immediately drop that question and conclude that it was a ridiculous question.

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So we just don't have the information to assess that, and that's part of the reason these case reports are not useful.
Q. The reports of rechallenges are numerous enough where the rechallenge resulted in resumption of symptoms, there are enough that you have to at least factor them into the analysis of general causation, correct? They have to be part of the analysis, correct?
A. They should be considered, absolutely. Everything that you can find, all data that are available should be considered, and these would be under that umbrella.
Q. The same would hold true for the dechallenges that were positive that showed the people getting better, that's also part of the data that should be analyzed in this question on general causation, correct?
A. Absolutely.
Q. Ultimately in forming an opinion on this, you can only go with the data that's available to you, correct?
A. Correct.
Q. And on a smaller scale, if you take a

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patient and you have information in a case report, you can only evaluate causation in that specific instance based on the information that is offered to you, that's available, correct?
A. That's right.
Q. So using the data that's available, there are case reports, you would agree with me, that based only on what is told in the case reports, that for some of those patients the most likely cause is olmesartan for their symptoms that correlate to the syndrome known as sprue-like enteropathy, correct?
MR. PARKER: Objection. Asked and answered.
A. No.
BY MR. SLATER:
Q. Is that because you're not comfortable crediting the rechallenge unless it's a controlled rechallenge?
A. That's because they haven't provided really much data about the dechallenge or rechallenge. Most of these say the patient felt better some days, months after stopping olmesartan, sometimes there's a biopsy. And in

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the rechallenge, usually it's anecdotal, and something along the lines in retrospect the patient restarted olmesartan because we didn't think of this and they got sicker again. So there's no -- you know, they're not well described. I think they could be better described, and that might help.
But in the end, they're not controlled. If they were controlled you, as we've been through, you could come up with a conclusion about specific causation if they were done in a controlled way. But just like drug efficacy, and one person doesn't prove that a drug is an efficacious drug in a general population, I don't think these dechallenge/rechallenge can be used in that way.
Q. Let's look at the Marthey study. Do you know that one? I think you listed that one as well.
A. Yes. Do you have it in your folders? Would that be an easier way to find it?
Q. I don't know if we sent it.
A. It should be here, but I'm not seeing it quickly. Let me look for a second. I'm

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sorry, I don't think I have it here. Let me just look a little more and be sure.
Q. We can send it. If you want to have it printed, we can have it sent down so you have it in front of you.
A. I'd like to be looking at it. Give me one more second.
MR. SLATER: Peter, I need to know if we sent you an article. It says "Images of the Month. Duodenal Villous Atrophy in a TTG-Negative Patient."
MR. FOUNDAS: Going through my index of what you sent over, it's not coming up.
MR. SLATER: I think it would have been e-mailed. This would have been in the pack that was --
MR. FOUNDAS: E-mailed later?
MR. SLATER: I don't know when it was sent. We're going to send two articles down to you. Let's go off the video for a second. We're going to send it to you guys, if you can tell us where to send it.
THE VIDEOGRAPHER: Going off the record. The time is 3:44.

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(Whereupon, a recess was taken.)
THE VIDEOGRAPHER: Back on the record. The time is 3:55.
BY MR. SLATER:
Q. Okay. You're looking at the Marthey article?
A. Yes.
Q. The Marthey article, and let's mark that one, if we could. Unless you want to wait until it gets -- we'll mark it when it comes in, they're bringing it in, so I'll make it easier. I don't want to steal, Mark, all your articles. You don't get all these free stickers, Doctor. I know that's what you thought this was all about, but you don't just get to keep all the stickers.
A. I'll have to go to my doctor's office then to get stickers, then.
Q. Okay. Looking at Marthey, this article was compiled by some French physicians requesting information from French gastroenterologists, correct?
A. Yes.
Q. And they were asked to report cases of

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olmesartan-associated enteropathy, and collect clinical, biological, and histological data. Patients with diarrhea and histological duodenal abnormalities were included, and they identified 36 patients, correct?

A. Yes.

(Whereupon, Turner Exhibit Number 17, Marthey, et al article titled Olmesartan-associated enteropathy: results of a national survey, was marked for identification.)

BY MR. SLATER:

Q. Now, going through what ultimately was done, there were ten patients who had a dechallenge and then continued to be followed, correct?

A. Correct.

Q. Of those ten patients, nine had remission, their symptoms went away, correct?

A. Correct.

Q. In all nine of those patients when the medication was reintroduced, their clinical symptoms relapsed, correct?

A. Correct.

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Q. So for those nine patients, you had a positive dechallenge in the sense that they got better when the drug was held, and then you had a positive rechallenge in the sense when the medication was restarted they got ill again, correct?

A. Again, with the same caveats we've been discussing, yes.

Q. This evidence needs to be considered in answering the question of whether there's general causation, it's a part of what needs to be considered, correct?

A. Correct.

Q. And if you go to Page 1107, which is the discussion, if you go down to the bottom right, the last paragraph says, "In conclusion, this study shows that olmesartan causes severe and potentially life-threatening enteropathy with or without villous atrophy." That's what the authors stated in this study, correct?

A. That's what they say.

Q. And they base that in large part on the fact that nine of the ten patients who had both a -- who had a dechallenge had success with

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the dechallenge, and that all nine of them had relapse with the rechallenge, correct?

A. Correct.

Q. Would you agree with me that for at least some number of those nine patients who had both a positive dechallenge and a positive rechallenge, that from a clinical perspective olmesartan was causing their gastrointestinal symptoms and villous atrophy?

A. No.

Q. Is that because this was not a controlled study that you give that answer?

A. It's because this is sort of a -- you know, it's an interesting study, but it's an incredibly weak collection, because there was nothing standardized about analysis of the patients at all.

Q. So basically if a study is not a controlled study where the patients were being controlled, regardless of what the outcome is, you will not give an opinion that there was causation even in the case of any of the patients being studied, because it doesn't reach the level of scientific rigor that you want to

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opine on, is that correct?

MR. PARKER: Objection.

A. I don't think that's exactly correct.

BY MR. SLATER:

Q. Okay. Let me -- my understanding is you're basically saying that unless you have a controlled study where the patient is being carefully followed, preferably in a randomized controlled setting, you're not comfortable relying on that data to make a finding of causation, am I correct?

A. I guess what I'm saying here is that this adds more of the same as the initial 2012 study where the authors concluded that there was not enough evidence. This is just increasing the number, but it doesn't add -- these are actually less rigorously evaluated than in the original Rubio-Tapia paper.

So I don't think you make a strong argument by increasing numbers. You make a strong argument -- we don't know how many patients this came from, we don't know how carefully they're worked up, because they were worked up all across France in all different

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places. So this ends up being less well-controlled. At least the Rubio-Tapia patients were all seen at Mayo. And that's where I just don't think this study can help you convince that it's a causative.

Q. In looking at the results, and I'm just working off of the summary at the start of the article, 29 of the 32 patients who had villous atrophy were in remission since olmesartan interruption, including 26 without immunosuppressants.

Do you see that?

A. Yes.

Q. That evidence is of enough significance that it should be considered in determining the question of whether there is general causation, that's part of what should be considered, correct?

A. For sure.

Q. Doctor, do you believe to a reasonable degree of medical certainty that the positive dechallenges and positive rechallenges that are discussed in this Marthey article are all coincidental to the withdrawal of olmesartan and

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the reuse of olmesartan as described? Is that your opinion?

A. My opinion is that some of these could be idiosyncratic drug reactions, some of these could be the result of something else they didn't pick up in their analyses, but that in none of these cases is there proof that olmesartan causes the enteropathy.

Q. You would agree with me that with regard to the patients who had the positive dechallenges and the positive rechallenges as discussed here, that it's possible that for at least some of those patients olmesartan was causing their clinical picture? You'll agree with that, correct?

A. It is possible. I would agree with that.

Q. You just would want to see more rigorous data in order to be willing for you to say I think it's likely, do I understand?

A. I think if you want to prove causation, you need stronger data than this, yes. I think anybody would agree with that.

MR. SLATER: Do we have that Kulai

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article?

MR. FOUNDAS: Yes.

(Whereupon, Turner Exhibit Number 18, Kulai, et al article titled Images of the Month. Duodenal Villous Atrophy in a TTG-Negative Patient Taking Olmesartan: A Case Report and Review of the Literature, was marked for identification.)

MR. SLATER: I'll tell you, Maureen, you are cranking today. Don't think it's not recognized, because it is.

All right. What I want to do actually is put Kulai to your side for one second, don't lose it, and pull out your report, Page 5. I want to cover something else, and then we'll get to this. And actually, I'm even going to wind you back a little more. Just one more question on Marthey.

A. Sure.

Q. With regard to the patients discussed in Marthey, do you have an opinion as to what was causing their intestinal symptoms as described? If it wasn't olmesartan, do you have

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an opinion as to what was causing it, as you sit here right now?

A. There's a range of things that could have been investigated in these patients. I can't tell you specifically in any case because, again, there's not sufficient data.

Q. Now, looking at your report, Page 5, at the very bottom, you state, "Although some of these studies have merit, it is also reasonable to conclude that Rubio-Tapia's small series stimulated investigators who were eager to join the phenomenon."

That's what you wrote, right?

A. Right.

Q. First of all, which of the studies have merit?

A. I think the studies we've been talking about have merit. The question is whether they prove causation. We disagreed on whether they proved causation. I don't think they're completely useless studies, they are of interest, they do bring people's attention to things.

Q. Now, are there any investigators you

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can point to who, as you say, were eager to join the phenomenon?
A. I think the most outrageous example would be Talbot.
Q. Anybody else that was eager to join the phenomenon?
A. I would have to go through them individually, but I think the effect is clear.
Q. I just want to know now as you sit here, other than Talbot, is there anyone you can point to and say this was somebody who was, you know, rushing in to join the phenomenon and publish something and, as you say, rigor wasn't applied, etcetera?
A. Why don't we go through them one at a time. Should we do that? I didn't prepare a list like that.
Q. Well, I just want to know, as you sit here now, if there's anybody other than Talbot that comes to mind?
A. I'm sure there are. Nobody specific that I can name. I know that if I look through the papers, many of the others have some of the same problems.

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Q. Is Marthey one of those?
A. Is who?
Q. The Marthey study. The Marthey article we just went through, do you think that was one where they rushed to join the phenomenon?
A. No, I think they have some level of rigor here. They did look and try to exclude other causes in this study.
Q. How about the Lagana study we went through?
A. Oh, that probably falls under the rush to publish something related to olmesartan heading.
Q. How about Greywoode?
A. Who?
Q. Greywoode.
A. I think Greywoode, again, is a case control study which is not as good as a randomized clinical trial, but it's something.
Q. What about DeGaetani?
A. I've got to find DeGaetani. Was DeGaetani an official exhibit?
MR. PARKER: No, it was not made an exhibit.

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BY MR. SLATER:
Q. That's the one where the Columbia celiac center went and recontacted patients.
A. I know which paper it is. I just want to look back. It's the seronegative villous atrophy paper.
Q. Exactly, where they identified 16 patients on olmesartan.
A. I'm sure they were stimulated to do that. I think it's an okay study. Again, I don't think it's proof. Here it is. I think it does have significant flaws.
Q. By the way, you said -- I'll withdraw that.
Okay. You then say, "Case reports continue to appear," and you list some of them going over to Page 6, right?
A. Yes.
Q. You don't criticize people publishing case reports about their experiences with patients that they relate to olmesartan, you would agree it's good for people to do that so they can increase the general knowledge of

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what's being seen clinically with patients, right?
MR. PARKER: Objection.
A. I don't think individual case reports like this really add much to general knowledge. If you want, I can quote my former chair on the topic.
BY MR. SLATER:
Q. Who is your former chair?
A. Ramzi Cotran.
Q. Did he play for the Cubs or the Red Sox?
A. No, he's sort of one of the most recognized pathologists in the world before his death.
Q. Okay. Kind of like Joseph Murray is one of the most recognized celiac specialists?
A. Not even close.
Q. No? Okay.
A. No. Cotran is way above Joe.
Q. Well, Cotran didn't write anything or do anything that had to do with olmesartan, did he?
A. I think he died before olmesartan was

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introduced to the market. But you were asking me about case reports, and he has wisdom on case reports.

Q. Okay. Well, there are a lot of doctors who are relying on case reports in evaluating and treating their patients, and a lot of these doctors think that this information is helping them to save patients from tremendous suffering, right?

MR. PARKER: Objection.

A. I think initial case reports bring attention to a problem or a potential problem. I think all these follow-on case reports are opportunities for people to publish something in the literature.

BY MR. SLATER:

Q. Have you ever published a case report?

A. I've been a co-author on some. I don't think I've initiated publication of a case report.

Q. Let's look at the Kulai case report.

By the way, I want to take a step back. One of the benefits of the case reports is to illustrate various clinical pictures for

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patients who may or may not be suffering from the condition being discussed, and that can be helpful to doctors to show them the range of potential presentations, that can be helpful, right?

A. That can be helpful, but it can also be harmful, because if you -- if these case reports are uncontrolled and you don't know what you're including, and you broaden and broaden what you accept as being published under this name, you'll end up with lots of people who don't fit, and are probably a completely different entity that may or may not be related to the drug in any way.

MR. SLATER: Move to strike from "but" forward.

Q. Let's look at the Kulai article we've marked as Exhibit 18. Okay?

A. Yes.

Q. This talks about a 68-year-old male who had a five-week history of nonbloody diarrhea, vomiting" --

THE VIDEOGRAPHER: I'm sorry, Mr. Slater, you're breaking up.

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MR. SLATER: Thank you.

Q. This talks about, looking at this article now, Exhibit 18, it's discussing a 68-year-old male with five-week history of nonbloody diarrhea, vomiting, and a 20 pound weight loss, correct?

A. Yes.

Q. It gives a great deal of information about his medical condition, including some new onset eye pain, said he had no fevers, no joint pain, no skin changes or recent travel. That's helpful information to help you give you a picture of this person's clinical presentation, correct?

A. Correct.

Q. It tells us "Past medical history included kidney stones, hypertension, and bioprosthetic aortic valve replacement three years earlier for severe aortic stenosis."

Again, this is helpful information giving a good clinical picture of the patient, correct?

A. Yes, I think they did a complete review of systems here.

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Q. "He had been on olmesartan/hydrochlorothiazide." You understand that's Benicar HCT? Did you know that?

A. Hydrochlorothiazide, but yes.

Q. He had been on that medication, Benicar HCT, for three to four years, right?

A. Yes.

Q. It then tells us his other medications, "ASA 81 milligrams twice weekly, vitamin C daily, multivitamin daily, cod liver oil daily, and acetaminophen as needed."

Do you see that list?

A. I do.

Q. Do any of those medications have a known risk to cause a five-week history of nonbloody diarrhea, vomiting, and a 20 pound weight loss?

A. I suppose it's possible that NSAIDs could.

Q. He takes the acetaminophen as needed. That's what it states, correct?

A. Acetaminophen is not an NSAID.

Q. I'll withdraw that question, obviously.

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Where do you see him taking NSAIDs?
A. ASA.
Q. Okay. Somebody taking ASA 81 milligrams twice weekly, would that be likely -- the likely cause of a patient with a five-week history of nonbloody diarrhea, vomiting, and a 20 pound weight loss?
A. No, it wouldn't be likely.
Q. Blood work was ordered, and they go through the findings on blood work, correct?
A. Correct.
Q. I'm not going to read all the findings, but do you see any findings on the blood work that would show an explanation for the five-week history of nonbloody diarrhea, vomiting, and a 20 pound weight loss?
A. In just the blood work, there is a metabolic acidosis, and there's an anemia that is normocytic, which is a little bit surprising if you're going to call it due to malabsorption, but that's all.
Q. Those findings could exist, the normocytic anemia and the metabolic acidosis, in somebody with malabsorption as well as this type

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of diarrhea, vomiting, and weight loss, that can happen, correct?
A. They could. Apparently they did. I would expect more of a macrocytic anemia.
Q. Just clarifying --
THE VIDEOGRAPHER: You broke up again.
Q. I'll ask again.
This presentation could exist, correct?
A. Yes. Apparently it did.
Q. The creatinine improved to 77, is that micromoles per liter, with intravenous fluid over five days?
A. Yes.
Q. "Stool was negative for culture, parasites, and Clostridium difficile," right?
A. Right.
Q. So it's good that they did stool cultures, that's helpful information to rule out potential causes, right?
A. Yes.
Q. The "TTG antibody was negative with normal immunoglobulin A levels."
That's helpful information, right?

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A. Yes.
Q. Biopsy was performed of the distal duodenum and duodenal cap revealing marked villous blunting with near complete villous atrophy of the small intestinal mucosa in some areas. That's important information, correct?
A. Correct.
Q. "There was an increase in intraepithelial lymphocytes as well as neutrophils in the surface epithelium." That information is important to help give us a full clinical picture, correct?
A. Well, that's the histopathologic picture, but yes.
Q. "The crypts had a prominent increase in apoptosis." That's, again, giving us histopathology, right?
A. Right.
Q. Then they tell us in the hospital, because he was hospitalized, that his uveitis, which would be basically an inflammation in his eye, that got better, right?
A. Right.
Q. He had a negative work up for

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syphilis, Lyme disease, sarcoid, and tuberculosis. So, again, more conditions were ruled out, right?
A. Right.
Q. And then we learn that "The patient's diarrhea resolved within two weeks of olmesartan discontinuation. His anemia improved to baseline and he returned to his previous weight within three months. Follow-up endoscopy 14 weeks later demonstrated complete resolution of the duodenal inflammatory changes and restoration of normal villous architecture," correct? That's what it states?
A. That's what it states.
Q. Now, this case report is quite detailed. Would you agree with that?
A. It's detailed, yeah.
Q. And based on the information here, the most likely cause of the five-week history of nonbloody diarrhea, vomiting, and a 20 pound weight loss, as well as the histopathologic findings, the most likely cause in this patient with all this information is olmesartan that he took in the form of Benicar HCT, correct?

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A. Well, using the published literature as my guide, this doesn't really fit the description, for example, that Rubio-Tapia wrote. So this is -- it could be, but this is actually a different histopathology.
Q. What is different about the histopathology here from the patients in Rubio-Tapia?
A. There are two features that I think are important that are discussed here. They discuss here intraepithelial neutrophils within the surface of the epithelium. Rubio-Tapia doesn't say anything about that. And a prominent increase in apoptosis, which is brought up much later in the literature, but is not in the Rubio-Tapia series. So I think they are bringing up something else. But again, it's a case report, and sort of a predatory publisher.
MR. SLATER: Okay. Move to strike.
Q. Doctor, you're not -- well, rephrase.
Is it your opinion that if olmesartan causes sprue-like enteropathy it must fit the clinical paradigm set forth in Rubio-Tapia 2012

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article, are you saying that's the only clinical picture that would fit that diagnosis if it exists?
A. No, I'm saying this doesn't fit that. And so this seems to be something potentially different from that.
Q. It could be that sprue-like enteropathy caused by olmesartan has that clinical and histopathological presentations, just like celiac disease does, right?
A. Celiac doesn't have this presentation.
Q. I didn't say celiac has this presentation. But celiac has very clinical and histopathologic presentations, correct?
A. You broke up partway through there. Can you repeat that?
Q. Let me ask the question clean.
You are not discounting the possibility that there are varied clinical and histopathologic presentations for olmesartan-associated enteropathy, you're not excluding that as a possibility, right?
A. I'm not excluding this histopathology as potentially being associated with olmesartan.

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Q. When you look at the evidence in this case as reported, which you've agreed is quite detailed, most likely cause for the diarrhea, the vomiting, and the 20 pound weight loss here, based on the published medical literature, would be the olmesartan? That's the most likely cause, correct?
A. As presented, that's what you're left with. But there's a number of things that would be important that are missing.
MR. SLATER: Move to strike from "but" forward.
Let's do this, because I just see it's 20 after 4:00. Let's go off the video.
THE VIDEOGRAPHER: Going off the record. The time is 4:22.
(Whereupon, a recess was taken.)
THE VIDEOGRAPHER: Back on the record. The time is 4:37.
BY MR. SLATER:
Q. Doctor, what medications would you say you would state to a reasonable degree of medical certainty cause a clinical syndrome similar to what has been put into the literature

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of olmesartan-associated enteropathy? What other medications?
A. Clinical syndromes, you're not exclusively talking about the histopathology?
Q. Combination of both.
A. Well, if you want to include the full range of what's been described with olmesartan, you could include methotrexate, mycophenolate, NSAIDs, ipilimumab, the list goes on. I mean, that's a good start.
Q. Okay. Let's start with those.
A. Tacrolimus would probably be in there.
Q. Let's talk about methotrexate.
A. Sure.
Q. Do you hold the opinion to a reasonable degree of medical certainty that in some patients methotrexate causes villous atrophy, severe diarrhea, weight loss?
A. Yes.
Q. Are there any case control studies you're relying on for that opinion?
A. I think they're pretty well-controlled studies. I don't know if they're case control studies. But there are animal studies, there's